

AMENDMENTS TO THE CLAIMS

1. - 129. (Canceled)

130. (New) A process useful for forming enantiomerically-enriched tetrahydrobiopterin (BH4) or a salt thereof from neopterin, comprising the steps of:

(a) reacting the primary hydroxyl group of neopterin with a silyl protecting group to form a silyl ether;

(b) protecting at least one secondary hydroxyl group of neopterin with at least one secondary hydroxyl protecting group;

(c) converting the silyl ether formed in step (a) to a surrogate group selected from the group consisting of halogens, sulfonates, and thioethers;

(d) reducing the surrogate group of step (c) to a methyl group; and

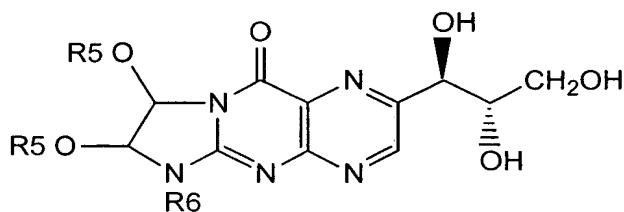
(e) removing the secondary hydroxyl protecting group(s) added in step (b).

131. (New) The process of claim 130, further comprising the steps of protecting the primary amine group at C-2 of neopterin with a 2-amino protecting group before performing step (a) and removing the 2-amino protecting group after performing step (a).

132. (New) The process of claim 131, wherein the 2-amino protecting group comprises a dialkylformamidedialkylacetal group or a pivaloyl derivative of neopterin.

133. (New) The process of claim 132, wherein the dialkylformamidedialkylacetal group is selected from the group consisting of N,N-dimethylformamidediethylacetal and N,N-dimethylformamidedimethylacetal.

134. (New) The process of claim 130, wherein the neopterin of step (a) comprises a compound of formula 20:



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wherein R5 is -COR';

R' is selected from the group consisting of a linear chain alkyl group, a branched chain alkyl group, an aryl group, and t-butyl; and

R6 is selected from the group consisting of a linear chain alkyl group, a branched chain alkyl group, and an aryl group.

135. (New) The process of claim 130, wherein said silyl protecting group of step (a) is selected from the group consisting of a linear chain alkyl substituted silyl group, a branched chain alkyl substituted silyl group, and an aryl substituted silyl group.

136. (New) The process of claim 135, wherein said silyl protecting group comprises a t-butyldimethylsilyl group or a t-butyldiphenylsilyl group.

137. (New) The process of claim 130, wherein at least one secondary protecting group comprises an acetal or a ketal.

138. (New) The process of claim 137, wherein the ketal comprises isopropylideneketal.

139. (New) The process of claim 130, wherein the surrogate group comprises a halogen, and wherein the converting of step (c) comprises reacting the silyl ether and a triphenylphosphine halogen.

140. (New) The process of claim 130, wherein the surrogate group comprises a sulfonate, and wherein the converting of step (c) comprises removing the silyl ether to form a primary hydroxyl group and sulfonating the resulting primary hydroxyl group.

141. (New) The process of claim 130, wherein the surrogate group comprises a thioether, and wherein the converting of step (c) comprises reacting the silyl ether and a mixture of (1) triphenylphosphine, (2) a dialkyl azodicarboxylate, and (3) a thiol.

142. (New) The process of claim 130, wherein the reducing of step (d) comprises reacting the surrogate of step (c) and a reducing agent comprising (1) Raney nickel and hydrogen or (2) sodium borohydride.

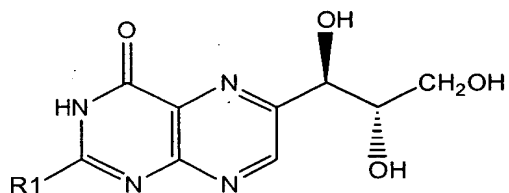
143. (New) The process of claim 130, further comprising the step of:

(f) performing an erythro-selective reduction of the product of step (e) to form BH4 or a salt thereof.

144. (New) The process of claim 143, further comprising

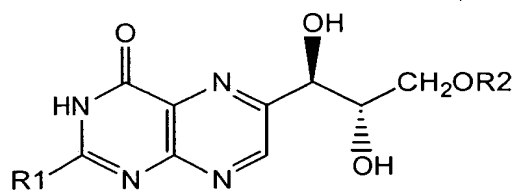
(g) crystallizing the BH4 salt.

145. (New) A compound having a formula:



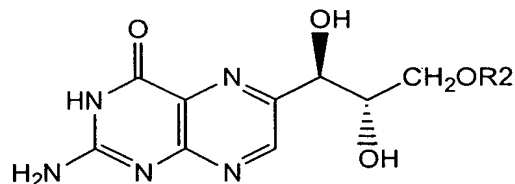
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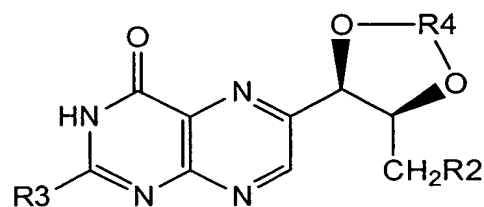
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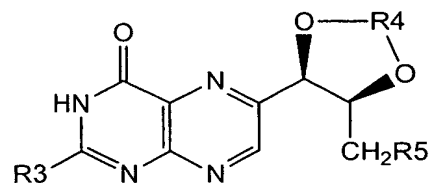


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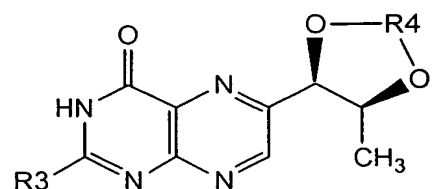


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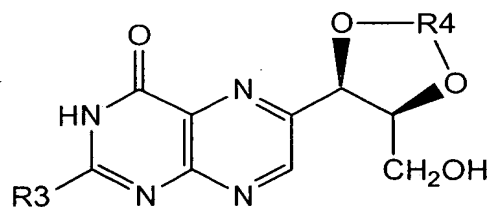


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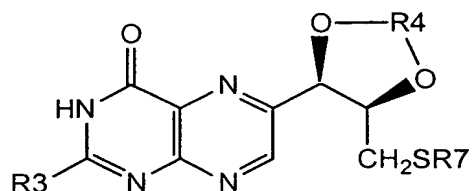


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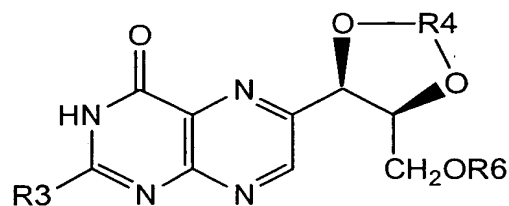
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11a

; or



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wherein R1 is selected from the group consisting of a single linear chain alkyl substituted amino group, a single branched chain alkyl substituted amino group, a double linear chain alkyl substituted amino group, a double branched chain alkyl substituted amino group, an aryl single substituted amino group, a linear chain alkyl substituted sulfur group, a branched chain alkyl substituted sulfur group, a single linear chain alkyl substituted alkylaminomethyleneimine group, a single branched chain alkyl substituted alkylaminomethyleneimine group, a double linear chain alkyl substituted alkylaminomethyleneimine group, a double branched chain alkyl substituted alkylaminomethyleneimine group;

R2 is a silyl group that is stable under acidic conditions;

R3 is selected from the group consisting of NH₂, 2,2-dimethylpropanamide, a single linear chain alkyl substituted amino group, a single branched chain alkyl substituted amino group, a double linear chain alkyl substituted amino group, a double branched chain alkyl substituted amino group, an single substituted amino group, a linear chain alkyl substituted sulfur group, and a branched chain alkyl substituted sulfur group;

R4 comprises a substituted acetal or ketal group that is stable under alkaline conditions;

R5 is a halogen;

R6 is selected from the group consisting of a linear chain alkyl substituted sulfonate, a branched chain alkyl substituted sulfonate, and an aryl substituted sulfonate; and

R7 is selected from the group consisting of a linear chain alkyl group, a branched chain alkyl group, and an aryl group.

146. (New) The compound of claim 145, wherein R2 is selected from the group consisting of diethylisopropylsilyl, dimethylisopropylsilyl, dimethylphenylsilyl, diphenylisopropoxysilyl, diphenyl-t-butoxysilyl, di-t-butylmethylsilyl, di-t-butylsilylene, methyldiisopropylsilyl, methyldiphenylsilyl, t-butylmethoxyphenylsilyl, t-butyl dimethylsilyl, hexyldimethylsilyl, triethylsilyl, 1,1,3,3-tetra-isopropylidisiloxane, triisopropylsilyl, trimethylsilyl, trimethylsilyloxycabomyl, and t-butyl diphenylsilyl.

147. (New) The compound of claim 145, wherein R4 is selected from the group consisting of methylene acetal, ethylidene acetal, t-butylmethylidene ketal, 1-t-butylethylidene ketal, 1-phenylethylidene ketal, 1-(4-methoxyphenyl)ethylidene acetal, 2,2,2-trichloroethylidene acetal, acrolein acetal, cyclopentylidene ketal, cyclohexylidene ketal, cycloheptylidene ketal, benzylidene acetal, p-methoxybenzylidene acetal, 2,4-dimethoxybenzylidene ketal, 3,4-dimethoxybenzylidene acetal, 2-nitrobenzylidene acetal, 4-nitrobenzylidene acetal, mesitylene acetal, 1-naphthaldehyde acetal, benzophenone ketal, and isopropylideneketal.

148. (New) The compound of claim 145, wherein R6 comprises a tosyl group.

149. (New) A process for forming enantiomerically-enriched tetrahydrobiopterin (BH4) or a salt thereof from a pterin, comprising the steps of:

- (a) substituting a pterin at the C-6 position to form a 6-substituted pterin;
- (b) protecting the primary amine group at C-2 of the 6-substituted pterin with an amino protecting group;
- (c) reacting the protected 6-substituted pterin of step (b) and a metalation reagent to form a metalation intermediate;
- (d) reacting the metalation intermediate and a lactic acid or a precursor of lactic acid;
- (e) removing the 2-amino protecting group of the product of step (d); and
- (f) performing an erythro-selective reduction to form BH4 or a salt thereof.

150. (New) The process of claim 149, wherein the 6-substituted pterin comprises a 6-halogenated pterin or a 6-sulfonated pterin.

151. (New) The process of claim 149, wherein the amino protecting group is selected from the group consisting of a single linear chain alkyl substituted amino group, a single branched chain alkyl substituted amino group, a double linear chain alkyl substituted amino group, a double branched chain alkyl substituted amino group, an aryl single substituted amino group, a linear chain alkyl substituted sulfur group, a branched chain alkyl substituted sulfur group, a linear chain alkyl single substituted amido group, a branched chain alkyl single substituted amido group, and an aryl substituted amido group.

152. (New) The process of claim 149, wherein the amino protecting group is selected from the group consisting of N,N-dimethylformamidediethylacetal, N,N-dimethylformamidedimethylacetal, and bis-dimethylamino-alkoxymethane.

153. (New) The process of claim 149, wherein the metalation reagent is selected from the group consisting of RMgX, an alkyl-metal complex, and a metal, wherein X is a halogen, and R is selected from the group consisting of an alkyl group and an aryl group.

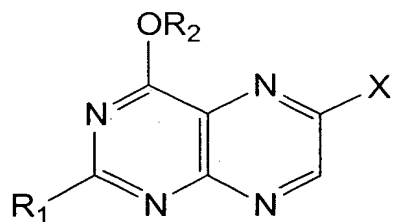
154. (New) The process of claim 153, wherein the metalation reagent is isopropyl magnesium chloride or an alkyl lithium complex.

155. (New) The process of claim 149, wherein the lactic acid of step (d) comprises a hydroxyl protected lactic acid chloride or the precursor of lactic acid of step (d) comprises 2-oxopropanoyl chloride or 2-oxopropanal.

156. (New) The process of claim 149, wherein the erythro-selective reduction comprises using (1) sodium borohydride in an alkaline medium or (2) hydrogen and a catalytic amount of platinum dioxide.

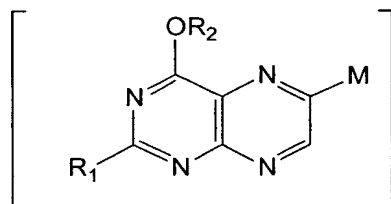
157. (New) The process of claim 149, further comprising the step of:
(g) crystallizing the BH₄ salt.

158. (New) A compound of having a formula:



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or

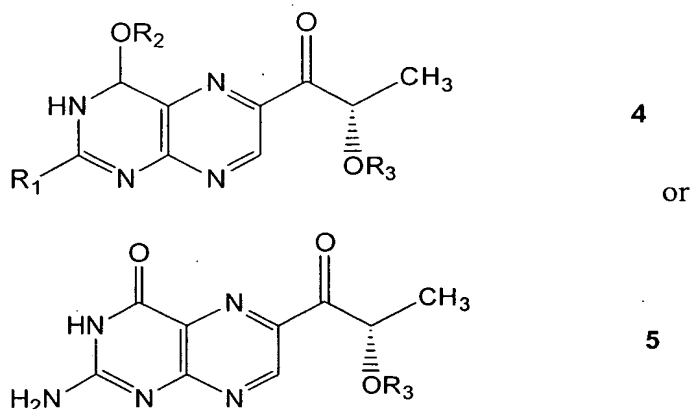


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wherein X is selected from the group consisting of chlorine, bromine, iodine, and a sulfonate; R₁ is selected from the group consisting of a single linear chain alkyl substituted amino group, a single branched chain alkyl substituted amino group, a double linear chain alkyl substituted amino group, a double branched chain alkyl substituted amino group, an aryl single substituted amino group, a linear chain alkyl substituted sulfur group, a branched chain alkyl substituted sulfur group, a single linear chain alkyl substituted alkylaminomethylene-imine group, a single branched chain alkyl substituted alkylaminomethylene-imine group, a double linear chain alkyl substituted alkylaminomethylene-imine group, and a double branched chain alkyl substituted alkylaminomethylene-imine group; R₂ is selected from the group consisting of hydrogen, a linear chain alkyl group, a branched chain alkyl group, and an aryl group; and M is selected from the group consisting of boron, silicon, zirconium, titanium, sodium, aluminum, nickel, cobalt, scandium, chromium, ytterbium, lithium, magnesium, zinc, palladium, copper, manganese, cesium, and tin.

159. (New) The compound of claim 158, wherein R₁ comprises an N,N-dimethylaminomethylene substituted amino group.

160. (New) A compound having a formula:



wherein R1 is selected from the group consisting of NH₂, 2,2-dimethylpropanamide, a single linear chain alkyl substituted amino group, a single branched chain alkyl substituted amino group, a double linear chain alkyl substituted amino group, a double branched chain alkyl substituted amino group, an aryl single substituted amino group, a linear chain alkyl substituted sulfur group, and a branched chain alkyl substituted sulfur group;
R2 is selected from the group consisting of hydrogen, a linear chain alkyl group, a branched chain alkyl group, and an aryl group; and
R3 is an acyl group.

161. (New) A process useful for forming enantiomerically-enriched tetrahydrobiopterin (BH₄) or a salt thereof from neopterin, comprising the steps of:

- (a) protecting the primary amine group at C-2 of neopterin with an amino protecting group;
- (b) converting the primary hydroxyl group of neopterin to a thioether; and
- (c) reducing the thioether of step (b) to a methyl group.

162. (New) The process of claim 161, wherein step (c) simultaneously further comprises removing the primary amine protecting group and performing an erythro-selective reduction to form BH₄ or a salt thereof.

163. (New) The process of claim 162, wherein the erythro-selective reduction comprises using Raney nickel and hydrogen.

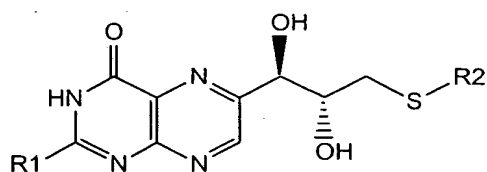
164. (New) The process of claim 161, further comprising the step of removing the primary amine protecting group after step (c).

165. (New) The process of claim 164, wherein the removing comprises reacting with zinc dichloride in ethanol.

166. (New) The process of claim 164, further comprising the step of performing an erythro-selective reduction to form BH4 or a salt thereof.

167. (New) The process of claim 166, wherein the erythro-selective reduction comprises using (1) sodium borohydride in an alkaline medium or (2) hydrogen and a catalytic amount of platinum dioxide.

168. (New) A compound having a formula:



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wherein R1 is selected from the group consisting of a single linear chain alkyl substituted amino group, a single branched chain alkyl substituted amino group, a double linear chain alkyl substituted amino group, a double branched chain alkyl substituted amino group, an aryl single substituted amino group, a linear chain alkyl substituted sulfur group, a branched chain alkyl substituted sulfur group, a single linear chain alkyl substituted alkylaminomethyleneimine group, a single branched chain alkyl substituted alkylaminomethyleneimine group, a double linear chain alkyl substituted alkylaminomethyleneimine group, and a double branched chain alkyl substituted alkylaminomethyleneimine group; and
R2 is selected from the group consisting of a linear chain alkyl group, a branched chain alkyl groups, and an aryl group.